

LISTING OF THE CLAIMS

1. (Currently amended) A combination which comprises an IBAT inhibitor, or a pharmaceutically acceptable salt, ~~soluate, solvate of such a salt or a prodrug~~ an in vivo hydrolysable ester or an in vivo hydrolysable amide thereof, and a metal salt, wherein the metal salt is formulated to release in the terminal ileum, caecum and/or the colon.
2. (Original) A combination according to claim 1 wherein the metal salt is a calcium salt.
3. (Previously Presented) A combination according to claim 1 wherein the metal salt is calcium phosphate.
4. (Withdrawn) A combination according to claim 1 wherein the IBAT inhibitor is a benzothiepine.
5. (Previously Presented) A combination according to claim 1 wherein the IBAT inhibitor is selected from:
 - 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(N-{{(R)-1'-phenyl-1'-[N'-(carboxymethyl)carbamoylethyl]carbamoylethoxy}-2,3,4,5-tetrahydro-1,5-benzothiazepine;
 - 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(N-{{(R)- α -[N'-(carboxymethyl)carbamoylethyl]-4-hydroxybenzyl]carbamoylethoxy}-2,3,4,5-tetrahydro-1,5-benzothiazepine;
 - 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(N-{{(R)-1'-phenyl-1'-[N'-(2-sulphoethyl)carbamoylethyl]carbamoylethoxy}-2,3,4,5-tetrahydro-1,5-benzothiazepine;
 - 1,1-dioxo-3-butyl-3-ethyl-5-phenyl-7-methylthio-8-(N-{{(R)-1'-phenyl-1'-[N'-(2-sulphoethyl)carbamoylethyl]carbamoylethoxy}-2,3,4,5-tetrahydro-1,5-benzothiazepine;
 - 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(N-{{(R)- α -[N'-(2-sulphoethyl)carbamoylethyl]-4-hydroxybenzyl]carbamoylethoxy}-2,3,4,5-tetrahydro-1,5-benzothiazepine;
 - 1,1-dioxo-3-butyl-3-ethyl-5-phenyl-7-methylthio-8-(N-{{(R)- α -[N'-(2-sulphoethyl)carbamoylethyl]-4-hydroxybenzyl]carbamoylethoxy}-2,3,4,5-tetrahydro-1,5-benzothiazepine;

- 1,1-dioxo-3-butyl-3-ethyl-5-phenyl-7-methylthio-8-(*N*-{(R)- α -[*N*-(2-carboxyethyl)carbamoyl]benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;
- 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(*N*-{(R)- α -[*N*-(2-carboxyethyl)carbamoyl]-4-hydroxybenzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;
- 1,1-dioxo-3-butyl-3-ethyl-5-phenyl-7-methylthio-8-(*N*-{(R)- α -[*N*-(5-carboxypentyl)carbamoyl]benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;
- 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(*N*-{(R)- α -[*N*-(2-carboxyethyl)carbamoyl]benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;
- 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(*N*-{ α -[*N*-(2-sulphoethyl)carbamoyl]-2-fluorobenzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;
- 1,1-dioxo-3-butyl-3-ethyl-5-phenyl-7-methylthio-8-(*N*-{(R)- α -[*N*-(R)-(2-hydroxy-1-carboxyethyl)carbamoyl]benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;
- 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(*N*-{(R)- α -[*N*-(R)-(2-hydroxy-1-carboxyethyl)carbamoyl]benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;
- 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(*N*-[(R)- α -(*N*'-(R)-1-[*N*'-(R)-(2-hydroxy-1-carboxyethyl)carbamoyl]-2-hydroxyethyl}carbamoyl]benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;
- 1,1-dioxo-3-butyl-3-ethyl-5-phenyl-7-methylthio-8-(*N*-{ α -[*N*'-(carboxymethyl)carbamoyl]benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;
- 1,1-dioxo-3-butyl-3-ethyl-5-phenyl-7-methylthio-8-(*N*-{ α -[*N*'-(ethoxy)(methyl)phosphorylmethyl]carbamoyl]benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;
- 1,1-dioxo-3-butyl-3-ethyl-5-phenyl-7-methylthio-8-(*N*-[(R)- α -(*N*'-{2-[(hydroxy)(methyl)phosphoryl]ethyl}carbamoyl]benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;
- 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(*N*-{(R)- α -[*N*'-(2-methylthio-1-carboxyethyl)carbamoyl]benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,5-benzothiazepine;
- 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(*N*-[(R)- α -(*N*'-{2-[(methyl)(ethyl)phosphoryl]ethyl}carbamoyl]-4-hydroxybenzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-

- 1,5-benzothiazepine;
- 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8- $\{N-[(R)-\alpha-(N^{\alpha}-\{2-[(methyl)(hydroxy)phosphoryl]ethyl\} carbamoyl)-4-hydroxybenzyl] carbamoylmethoxy\}-2,3,4,5-tetrahydro-1,5-benzothiazepine;$
- 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8- $\{N-[(R)-\alpha-[(R)-N^{\alpha}-(2-methylsulphinyl-1-carboxyethyl) carbamoyl]benzyl\} carbamoylmethoxy\}-2,3,4,5-tetrahydro-1,5-benzothiazepine;$ and
- 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methoxy-8- $[N-\{(R)-\alpha-[N^{\alpha}-(2-sulphoethyl) carbamoyl]-4-hydroxybenzyl\} carbamoylmethoxy]-2,3,4,5-tetrahydro-1,5-benzothiazepine;$
- or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof.
6. (Withdrawn) A combination according to claim 1 wherein the IBAT inhibitor is selected from:
- 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8- $\{N-[(R)-\alpha-[N-((R)-1-carboxy-2-methylthioethyl) carbamoyl]-4-hydroxybenzyl\} carbamoylmethoxy\}-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepine;$
- 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8- $\{N-[(R)-\alpha-[N-((S)-1-carboxy-2-(R)-hydroxypropyl) carbamoyl]-4-hydroxybenzyl\} carbamoylmethoxy\}-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepine;$
- 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8- $\{N-[(R)-\alpha-[N-((S)-1-carboxy-2-methylpropyl) carbamoyl]-4-hydroxybenzyl\} carbamoylmethoxy\}-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepine;$
- 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8- $\{N-[(R)-\alpha-[N-((S)-1-carboxybutyl) carbamoyl]-4-hydroxybenzyl\} carbamoylmethoxy\}-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepine;$
- 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8- $\{N-[(R)-\alpha-[N-((S)-1-carboxypropyl) carbamoyl]benzyl\} carbamoylmethoxy\}-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepine;$
- 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8- $\{N-[(R)-\alpha-[N-((S)-1-carboxyethyl) carbamoyl]benzyl\} carbamoylmethoxy\}-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepine;$
- 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8- $\{N-[(R)-\alpha-[N-((S)-1-carboxy-2-(R)-hydroxypropyl) carbamoyl]benzyl\} carbamoylmethoxy\}-2,3,4,5-tetrahydro-1,2,5-$

- benzothiadiazepine;
- 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(*N*-{(R)- α -[*N*-(2-sulphoethyl)carbamoyl]-4-hydroxybenzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepine;
- 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(*N*-{(R)- α -[*N*-(*S*)-1-carboxyethyl]carbamoyl]-4-hydroxybenzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepine;
- 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(*N*-{(R)- α -[*N*-((R)-1-carboxy-2-methylthioethyl)carbamoyl]benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepine;
- 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(*N*-{(R)- α -[*N*-(*S*)-1-[*N*-((*S*)-2-hydroxy-1-carboxyethyl)carbamoyl]propyl}carbamoyl]benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepine;
- 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(*N*-{(R)- α -[*N*-(*S*)-1-carboxy-2-methylpropyl]carbamoyl]benzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepine;
- 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-(*N*-{(R)- α -[*N*-((*S*)-1-carboxypropyl)carbamoyl]-4-hydroxybenzyl}carbamoylmethoxy)-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepine; and
- 1,1-dioxo-3,3-dibutyl-5-phenyl-7-methylthio-8-[*N*-((R)- α -carboxy-4-hydroxybenzyl)carbamoylmethoxy]-2,3,4,5-tetrahydro-1,2,5-benzothiadiazepine;
- or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof.

7. – 8. (Cancelled)

9. (Withdrawn) A method for producing an IBAT inhibitory effect in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective amount of a combination according to claim 1.

10. (Withdrawn) A method of preventing diarrhoea that would result from excess bile acids in the intestine following administration of an effective amount an IBAT inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, to a warm

blooded animal, such as man, in need of such treatment, which comprises administering to said animal an effective amount of a combination according to claim 1.

11. (Previously Presented) A pharmaceutical composition which comprises a combination according to claim 1, in association with a pharmaceutically acceptable diluent or carrier.

12. – 14. (Cancelled)

15. (Withdrawn) A method of treating hyperlipidaemic conditions in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective amount of a combination according to claim 1.

16. – 18. (Cancelled)

19. (Previously Presented) The combination according to claim 1 further comprising an HMG Co-A reductase inhibitor, or pharmaceutically acceptable salts, solvates, solvates of such salts or prodrugs thereof.

20. (Original) The combination according to claim 19 wherein the HMG Co-A reductase inhibitor is fluvastatin, lovastatin, pravastatin, simvastatin, atorvastatin, cerivastatin, bervastatin, dalvastatin, mevastatin and rosuvastatin, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof.

21. (Withdrawn) The combination according to claim 1 further comprising a cholesterol absorption antagonist, or pharmaceutically acceptable salts, solvates, solvates of such salts or prodrugs thereof.

22. (Withdrawn) The combination according to claim 21 wherein the a cholesterol absorption antagonist is SCH 58235.

23. (Withdrawn) The combination according to claim 1 further comprising a PPAR alpha and/or gamma agonist, or pharmaceutically acceptable salts, solvates, solvates of such salts or prodrugs thereof.

24. (Withdrawn) The combination according to claim 23 wherein the PPAR alpha and/or gamma agonist is (S)-2-ethoxy-3-[4-(2-{4-methanesulphonyloxyphenyl}ethoxy)phenyl]-propanoic acid and pharmaceutically acceptable salts thereof.

25. – 26. (Cancelled)

27. (Withdrawn) A method for producing an IBAT inhibitory effect in a warm-blooded animal, such as man, in need of such treatment which comprises administering to said animal an effective amount of a composition according to claim 19.

28. (Previously Presented) A pharmaceutical composition which comprises a combination according to claim 19, in association with a pharmaceutically acceptable diluent or carrier.

29. – 31. (Cancelled)

32. (Withdrawn) A method of preventing diarrhoea that would result from excess bile acids in the intestine following administration of an IBAT inhibitor, or a pharmaceutically acceptable salt, solvate, solvate of such a salt or a prodrug thereof, which comprises administering to a patient in need thereof, a metal salt, wherein the metal salt is formulated to release in the terminal ileum, caecum and/or the colon.